Listing of Claims

1. (previously presented) A method for preparing small particles of a poorly water soluble pharmaceutically active compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent that is aqueous, the method comprising: (i) dissolving the poorly water soluble pharmaceutically active compound in the water-miscible first solvent to form a solution; (ii) mixing the solution with the second solvent to form a mix; and (iii) simultaneously homogenizing the mix and continuously removing the first solvent from the mix to form an aqueous suspension of small particles having an average effective particle size of from about 10 nm to about 100 µm wherein the aqueous suspension is essentially free of the first solvent.

2. (original) The method of claim 1, wherein the water-miscible first solvent is a protic organic solvent.

3. (original)The method of claim 2, wherein the protic organic solvent is selected from the group consisting of alcohols, amines, oximes, hydroxamic acids, carboxylic acids, sulfonic acids, phosphonic acids, phosphoric acids, amides and ureas.

4. (original) The method of claim 1, wherein the water-miscible first solvent is an aprotic organic solvent.

5. (original) The method of claim 4, wherein the aprotic organic solvent is a dipolar aprotic solvent.

6. (original) The method of claim 5, wherein the dipolar aprotic solvent is selected from the group consisting of fully substituted amides, fully substituted ureas, ethers, cyclic ethers, nitriles, ketones, sulfones, sulfoxides, fully substituted phosphates, phosphonate esters, phosphoramides, and nitro compounds.

7. (original) The method of claim 1, wherein the water-miscible first solvent is selected from the group consisting of N-methyl-2-pyrrolidinone (N-methyl-2-pyrrolidone), 2-pyrrolidinone (2-pyrrolidone), 1, 3-dimethyl-2-imidazolidinone (DMI), dimethylsulfoxide, dimethylacetamide, acetic acid, lactic acid, methanol, ethanol, isopropanol, 3-pentanol, n-propanol, benzyl alcohol, glycerol, butylenes glycol (butanediol), ethylene glycol, propylene glycol, mono-and diacylated monoglycerides, glyceryl caprylate, dimethyl isosorbide, acetone, dimethylsulfone, dimethylformamide, 1,4-dioxane, tetramethylenesulfone (sulfolane), acetonitrile, nitromethane, tetramethylurea, hexamethylphosphoramide (HMPA), tetrahydrofuran (THF), dioxane, diethylether, tert-butyhnethyl ether (TBME), aromatic hydrocarbons, alkenes, alkanes, halogenated aromatics, halogenated alkenes, halogenated alkanes, xylene, toluene, benzene, substituted benzene, ethyl acetate, methyl acetate, butyl acetate, chlorobenzene, bromobenzene, chlorotoluene, trichloroethane, methylene chloride, ethylenedichloride (EDC), hexane, neopentane, heptane, isooctan, cyclohexane, polyethylene glycol (PEG), PEG-4, PEG-8, PEG-9, PEG-12, PEG-14, PEG-16, PEG- 120, PEG-75, PEG-150, polyethylene glycol esters, PEG-4 dilaurate, PEG-20 dilaurate, PEG-6 isostearate, PEG-8 palmitostearate, PEG-150 palmitostearate, polyethylene glycol sorbitans, PEG-20 sorbitan isostearate, polyethylene glycol monoalkyl ethers, PEG-3 dimethyl ether, PEG-4 dimethyl ether, polypropylene glycol (PPG), polypropylene alginate, PPG-10 butanediol, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-15 stearyl ether, propylene glycol dicaprylate/dicaprate, propylene glycol laurate, and glycofurol (tetrahydrofurfuryl alcohol polyethylene glycol ether).

8. (previously presented) The method of claim 1, wherein the water-miscible first solvent is N-methyl-2-pyrrolidinone.

9. (previously presented) The method of claim 1, wherein the water-miscible first solvent is lactic acid.

10. (original) The method of claim 1 further comprising mixing into the water-miscible first solvent or the second solvent or both the water-miscible first solvent and the second solvent one or more surface modifiers selected from the group consisting of: anionic surfactants, cationic surfactants, nonionic surfactants and surface active biological modifiers.

11. (original) The method of claim 1, wherein the removal of the first solvent is by filtration.

12. (original) The method of claim 11, wherein the filtration is cross-flow ultrafiltration.

13. (original) The method of claim 12, wherein the ultrafiltration comprises concentrating the mix to form a concentrate and diafiltering the concentrate to remove the first solvent.

14. (original) The method of claim 11, wherein a polymeric membrane filter is used for the ultrafiltration.

15. (original) The method of claim 11, wherein a ceramic membrane filter is used for the ultrafiltration.

16. (original) The method of claim 1, wherein the first solvent is present in the aqueous suspension at less than about 100 ppm.

17. (original) The method of claim 1, wherein the first solvent is present in the aqueous suspension at less than about 50 ppm.

18. (original) The method of claim 1, wherein the first solvent is present in the aqueous suspension at less than about 10 ppm.

19. (cancelled).

20. (previously presented) The method of claim 1, wherein the poorly water soluble pharmaceutically active compound has a solubility in water of less than about 10 mg/mL.

21. (cancelled)

22. (previously presented) The method of claim 1, wherein the pharmaceutically active compound is itraconazole.

23. (previously presented) The method of claim 1, wherein the pharmaceutically active compound is budesonide.

24. (currently amended) The method of claim 1, wherein the pharmaceutically active ~~agent~~ compound is carbamazepine.

25. (currently amended) The method of claim 1, wherein the pharmaceutically active ~~agent~~ compound is prednisolone.

26. (currently amended) The method of claim 1, wherein the pharmaceutically active ~~agent~~ compound is nabumetone.

27. (cancelled)

28. (previously presented) The method of claim 1, wherein the small particles have an average effective particle size of from about 10 nm to about 10 μm.

29. (previously presented) The method of claim 1, wherein the small particles have an average effective particle size of from about 10 nm to about 2 μm.

30. (previously presented) The method of claim 1, wherein the small particles have an average effective particle size of from about 10 nm to about 1 μm.

31. (previously presented) The method of claim 1, wherein the small particles have an average effective particle size of from about 50 nm to about 400 nm.

32. (previously presented) The method of claim 1, wherein the small particles have an average effective particle size of from about 50 nm to about 200 nm.

33. (original) The method of claim 1, further comprising sterilizing the aqueous suspension.

34. (original) The method of claim 33, wherein sterilizing the aqueous suspension comprises sterile filtering the solution and the second solvent before mixing and carrying out the subsequent steps under aseptic conditions.

35. (previously presented) The method of claim 33, wherein sterilizing comprises heat sterilization.

36. (original) The method of claim 35, wherein the heat sterilization is effected within the homogenizer in which the homogenizer serves as a heating and pressurization source for sterilization.

37. (original) The method of claim 33, wherein sterilizing comprises the gamma irradiation.

38. (original) The method of claim 1 further comprising removing the aqueous phase of the aqueous suspension to form a dry powder of the small particles.

39. (original) The method of claim 38, wherein removing the aqueous phase is selected from the group consisting of: evaporation, rotary evaporation, lyophilization, freeze-drying, diafiltration, centrifugation, force-field fractionation, high-pressure filtration, and reverse osmosis.

40. (original) The method of claim 38 further comprising the step of adding a diluent to the small particles.

41. (original) The method of claim 40, wherein the diluent is suitable for parenteral administration of the particles.

42. (original) A composition of small particles prepared by the method of claim 1.

43. (previously presented) The composition of claim 42 administered to a subject in need of the composition by a route selected from the group consisting of parenteral, oral, pulmonary, topical, ophthalmic, nasal, buccal, rectal, vaginal, and transdermal.

44. (original) The method of claim 1 wherein the solution and the second solvent are mixed while simultaneously homogenizing the mix and continuously removing the first solvent from the mix.

45. (currently amended) The [[A]] method of claim 1, wherein said ~~for preparing small particles of a poorly water-soluable pharmaceutically active compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent that is aqueous, the method comprising: (i) dissolving the poorly water soluble pharmaceutically active compound in the water-miscible first solvent to form a solution (ii) mixing the solution with the second solvent to form a mix; and (iii) simultaneously homogenizing the mix and~~ continuously removing the first solvent from the mix is by cross-flow ultrafiltration ~~to form an aqueous suspension of small particles having an average effective particle size of from about 10 nm to about 100 µm wherein the aqueous suspension is essentially free of the first solvent~~.

46. (previously presented) A method for preparing small particles of a poorly water-soluble pharmaceutically active compound, the solubility of which is greater in a water-miscible first solvent than in a second solvent that is aqueous, the method comprising: (i) dissolving the poorly water-soluble pharmaceutically active compound in the water-miscible first solvent to form a solution; and (ii)

simultaneously mixing the solution with the second solvent to form a mix while homogenizing the mix and continuously removing the first solvent from the mix to form an aqueous suspension of small particles having an average effective particle size of from about 10 nm to about 100 μm wherein the aqueous suspension is essentially free of the first solvent.

47. (previously presented) The method of claim 1, wherein said pharmaceutically active compound is selected from the group consisting of therapeutic agents, diagnostic agents, nutritional supplements, and combinations thereof.

48. (previously presented) The method of claim 1, wherein the small particles have an average effective particle size of from about 10 nm to about 20 μm.

49. (new) A method for preparing small particles of a poorly water soluble pharmaceutically active compound selected from the group consisting of itraconazole, carbamazepine, nabumetone, budenoside, prednisolone and combinations thereof, the solubility of which is greater in a water-miscible first solvent than in a second solvent that is aqueous, the method comprising: (i) dissolving the poorly water soluble pharmaceutically active compound in the water-miscible first solvent to form a solution; (ii) mixing the solution with the second solvent to form a mix; and (iii) simultaneously homogenizing the mix and continuously removing the first solvent from the mix to form an aqueous suspension of small particles having an average effective particle size of from about 10 nm to about 100 μm wherein the aqueous suspension is essentially free of the first solvent.